

REMARKS/ARGUMENTS

Claims 1-2, 8-40, and 46-67 are currently pending and under examination in the application.

Claims 3-7 and 41-45 have been withdrawn by the Examiner as being directed to non-elected subject matter. Applicants reserve the right to present this subject matter in a co-pending application.

Claims 62-67 have been newly added as a result of this Amendment. Claim 62 recites "a dose of about 200 mg." Claim 63 recites "a dose of about 300 mg." Claim 64 recites "a dose of about 400 mg." Claim 65 recites "a dose of about 200 mg." Claim 66 recites "a dose of about 300 mg." Claim 67 recites "a dose of about 400 mg" (see, *inter alia*, page 10, lines 6-14; and page 14, lines 9-31 to page 15, lines 1-10 of the application as originally filed).

These amendments are supported by the application as originally filed, and do not constitute new matter. Support for the amendments is shown in parentheses, above. Entry of these amendments is respectfully requested.

RELATED CASES

The Examiner has requested a listing of the co-pending and related U.S. cases of inventor Thomas A. Miller (Office Action, page 3). Applicants have provided herewith a Supplemental Information Disclosure Statement and PTO Form 1449 which present these published U.S. applications for review by the Examiner. Applicants also point to U.S. Patent No. 6,511,990 which was filed with the Information Disclosure Statement on April 6, 2004. In addition, U.S. Publication No. 2004/0127523 was filed with the Supplemental Information Disclosure Statement on March 14, 2005. Applicants present also U.S. Publication No. 2004/0072735 for review by the Examiner. Applicants note that U.S. Publication No. 2004/0087631 corresponds to the instant application.

35 U.S.C. §132

The Examiner has objected to the Amendment file December 22, 2003 under 35 U.S.C. §132 as allegedly introducing new matter into the disclosure (Office Action, page 3). The Examiner states that certain phrases and terms were not supported by the application as filed. *Id.* Applicants respectfully traverse this rejection as follows.

Regarding recitation of “cell growth arrest and/or apoptosis,” this phrase is supported by the application as originally filed (see, *inter alia*, page 1, lines 17-23, page 4, lines 25-27, and page 6, lines 27-29 of the application).

Regarding recitation of “crystal structures” and “amorphous structures,” these phrases are supported by the application as originally filed (see, *inter alia*, page 46, lines 14-15 of the application).

Regarding recitation of “derivatives,” this term is supported by the application as originally filed (see, *inter alia*, page 7, lines 11-12, page 20, lines 10-24, and page 21, lines 5-25 of the application).

Regarding recitation of “depudecin,” this term is supported by the application as originally filed (see, *inter alia*, page 9, line 26 and page 13, lines 6-7 of the application).

Regarding recitation of “and/or the anti-cancer agents,” this phrase is supported by the application as originally filed (see, *inter alia*, page 17, lines 2-4 and page 46, lines 21-26 of the application).

Applicant believes that the amendments to the specification are supported by the disclosure of the application as filed. Withdrawal of this objection is respectfully requested.

35 U.S.C. §103(a)

Claims 1, 2, 8-40, and 46-61 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Jackson *et al.* (US 2003/0161830; “Jackson”; Office

Action, page 4). The Examiner states that, based on Jackson, one of skill in the art would have been motivated to treat mesothelioma by the administration of SAHA, and contends that the determination of an optimal dosing regimen involves no more than routine experimentation. *Id.*

Applicants traverse.

Jackson is deficient. Jackson merely provides a long list of HDAC inhibitors, including trichostatin A, trapoxin/trapoxin A, CHAPs, MS-27-275, SAHA, depsipeptide (FR901228; FR228), CI-994, CBHA, pyroxamide, CHAP31, HC-toxin, chlamydocin, Cly-2, WF-3161, Tan-1746, apicidin, and analogs (see, e.g., ¶¶ [0008], [0217]). The majority of these HDAC inhibitors are not hydroxamic acids. Jackson provides an even longer list of potential diseases for treatment, including more than 168 types of cancers (only one of which is mesothelioma), a number of inflammatory illnesses, and several degenerative disorders (~200 total diseases; see, e.g., ¶¶ [0205] - [0217]). Out of more than 3400 possible combinations of the agents and potential diseases (~200 diseases x >17 HDAC inhibitors and analogs), Jackson provides no teaching or suggestion to select the specific HDAC inhibitors, *hydroxamic acids*, for treatment of the specific disease of *mesothelioma*. The Examiner provides no other references to motivate the selection of the specific treatment modality claimed here.

The Examiner argues that the selection of SAHA to treat mesothelioma would be obvious to one of skill in the art. However, the mere fact that this combination *can* be made out of more than 3400 choices is not sufficient to establish obviousness. *See In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990); MPEP §2143.01. Because elements are capable of an infinity of permutations, the selection of a particular combination is key, and “[i]t is the act of selection that is the invention...” (emphasis added). *B.G. Corp. v. Walter Kidde & Co.*, 79 F.2d 20, 22 (2d Cir. 1935). It is the particular choice and combination of elements in an invention that is the critical inquiry. *Reeves Instruments v. Beckmann Instruments*, 444 F.2d 263, 270 (9th Cir. 1971); *Republic Industries v. Schlage Lock Co.*, 592 F.2d 963, 970 (7th Cir. 1979). There must be independent suggestion to

make the combination without the slightest recourse to Applicants' teachings. *Id.* Otherwise the references in the field are inviting unguided and speculative experimentation which is not the standard for 35 U.S.C. §103. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 18 U.S.P.Q.2d, 1016, 1022 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988).

In the instant case, Applicants have selected the specific combination of hydroxamic acids with mesothelioma. Applicants have recognized that hydroxamic acid HDAC inhibitors have roughly equal potency in inhibiting multiple histone deacetylases. Applicants have realized the importance of such broad spectrum HDAC inhibition and shown that hydroxamic acid HDAC inhibitor is effective for treatment of mesothelioma (see, *inter alia*, Example 5 and Figure 13 of the application as originally filed). Jackson fails to recognize the distinctive capabilities of hydroxamic acids and their specific use for treatment of mesothelioma. In fact, Jackson presents no instructions regarding which HDAC inhibitors to use for which types of diseases. Given the lack of guidance presented by Jackson, one of skill in the art could not have used "routine experimentation" to modify Jackson and arrive at Applicants' invention as claimed. At best, Jackson invites the reader to try various, random combinations (more than 3400 possibilities) of HDAC inhibitors and diseases. This is not the accepted benchmark for obviousness. See, e.g., *In re Goodwin*, 576 F.2d 375, 377 (C.C.P.A. 1978); *In re Geiger*, 815 F.2d 686, 688 (Fed. Cir. 1987).

For at least these reasons, the subject matter of claims 1, 2, 8-40, and 46-61 cannot be considered obvious in view of Jackson. Withdrawal of this rejection is respectfully requested.

CONCLUSION

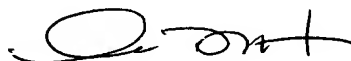
A favorable action on the merits is respectfully requested. If any discussion of this Amendment would be deemed helpful, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

U.S. Serial No. 10/650,025
Applicants: Bacopoulos *et al.*

Applicants believe no further fee is due at this time; however, the Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. **50-0311**, Reference Number: **24852-501 CIP3** (Customer Number: **35437**).

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Respectfully submitted,



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